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10/699,521	10/31/2003	Guohua Chen	ALZA-0129	4222

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EXAMINER	
SILVERMAN, ERIC E	
ART UNIT	PAPER NUMBER
1618	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/699,521	CHEN ET AL.	
	Examiner	Art Unit	
	Eric E. Silverman, PhD	1618	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *22 January 2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-122* is/are pending in the application.

4a) Of the above claim(s) *14-17,21,54-56 and 73-121* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-13,18-20,22-53,57-72 and 122* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *1-3-06,2-9-04*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Applicants' response, filed 1/22/2007, is noted. Claims 1 - 122 are pending.

Election/Restrictions

Applicant's election with traverse of Group I, claims 1 – 72 and 122, in the reply filed on 1/22/2007 is acknowledged. The traversal is on the ground(s) that the Office action does not give an appropriate explanation of the reason for serous burden. Applicant avers that the proffered explanation is merely a recitation of sections of the MPEP, and is not appropriate. This is not found persuasive because the explanation provided is considered appropriate according to current USPTO policies and procedures, and indeed the proffered explanation is currently a form paragraph approved for use by examiners as an explanation of burden in restriction requirements.

The requirement is still deemed proper and is therefore made **FINAL**.

Applicants' election of the polymer PLGA and the solvent benzyl alcohol as species of the invention is acknowledged. Because Applicants did not aver any error in the requirement for an election of species, and as such the election of species is being treated as an election **without traverse**. Applicants indicated that claims 1 - 13, 18 – 20, 22 – 53, 57 – 109, 11 [sic: 111] – 122 as readable on the elected species.

Accordingly claims 1 – 13, 18 – 20, 22 – 53, 57 – 72, and 122 are treated on the merits below, and claims 14 – 17, 21, 54 – 56, and 73 – 121 are withdrawn as reading on a non-elected invention or species.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1 – 13, 18 – 20, 22 – 24, 28 – 39 and 122 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Independent claims 1, and 122 recite a "low molecular weight" polymer. Absent a definition in the specification, it is not clear what molecular weights are "low" as claimed. The artisan would thus be unable to determine the metes and bounds of the invention.

The remaining claims are rejected for ultimately depending on claim 1 without clarifying this issue.

Claim Rejections - 35 USC § 102

> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1 – 7, 10 – 12, 18 – 20, 22, 24,29 - 35, 40 - 52, 57 - 65, 70and 72 are rejected under 35 U.S.C. 102(b) as being anticipated by US 6,130,200 to Brodbeck et al. of record

Claim 1 requires a sustained release dosage form, which is a gel comprising a low molecular weight bioerodibe polymer, a water-immiscible solvent in amount sufficient to form a gel with the polymer, and an anesthetic dissolved or dispersed in the gel.

The elected polymer is PLGA, and the elected solvent is benzyl alcohol.

Claims 2 - 4 relate to the efficacy ratio of claim 1's composition. It is understood that the composition of claim 1 would necessarily have these ratios. Claims 5 – 7 relate to the sustained release rate of claim 1. Claim 7 requires that sustained release last from about 24 hours to about 7 days. Claims 10 - 12 relate to the solvents of claim 1. Claim 10 requires a solvent having a miscibility in water less than 7 wt.% at 25C, and claim 11 forbids inclusion of any solvent having a greater miscibility. Claims 18 - 20 and 22 relate to the polymer, and read on the elected PLGA polymer. Claim 24 requires the polymer to have carboxylic acid end groups. It is understood that unmodified PLGA, being a polyester, has carboxylic acid end groups. Claims 25 - 28 relate to the polymers' molecular weight average molecular weight, with the most limiting claim (claim 28) requiring a molecular weight of about 5,000. Claims 29 – 31 relate to the amount of anesthetic, with claim 31 requiring the anesthetic to be present in about 1% to about 30% by weight. Claims 32 – 34 relate to the ratio of polymer and solvent, with claim 34 requiring the ratio to be between 30:70 and 75:25. Claim 35 requires an additional material, such as an excipient.

Claim 40 is similar to claim 1, but it additionally requires that the polymer be a lactic-acid based polymer, and that the weight average molecular weight be from about 3,000 to about 10,000. Claims 41 – 52, 57 – 65, and 72 are similar to the claims discussed above, except that they ultimately depend from claim 40 instead of claim 1.

Brodbeck teaches a composition that is a PLGA copolymer gel with a solvent present in amounts effective to plasticize the gel. Claim 1. The solvent has a miscibility in water of less than 7%. Claim 2. The solvent may be benzyl benzoate. Claim 3.

Benzyl benzoate is a recognized topical analgesic. See US 6,673,363 at claim 20. The sustained release, in some embodiements, occurs in a period of between about 24 hours and about 7 days. See Figure 2, plot with squares, and description thereof. When a mixture of solvents is used, such as 80/20 benzyl benzoate/triacetin or 80/20 benzyl benzoate/NMP, neither solvent has a miscibility in water of more than 7% by weight. See e.g. col. 13 lines 13 - 50. PLGA, being the elected polymer, is admitted to read on the polymer of instant claims 18, 19, and 22. Example 1 of the art shows 50:50 lactide:glycolide in the polymer, as per instant claim 20. As discussed above, when PLGA is not modified, it necessarily comprises carboxylic acid end groups, being a polyester. An exemplified PLGA molecular weight is 5,000. Col. 11, lines 23 – 41. The dosage form comprises, for example, 50% solvent and 50% polymer. Col. 14, lines 43 - 67. The solvent is, for example, 80:20 benzyl benzoate/triacetin. Col. 14, 43 - 67. As such the benzyl benzoate (anesthetic) is present in 40% of the final product by weight (50% product being solvent and 80% of the solvent being benzyl benzoate). 40% by weight reads on instant claims 29 - 30 literally, and is understood to be included in "about 30% by weight" recited in instant claim 31, because there is no specific definition of the limits of about, and the anesthetic would be expected to have the same or similar properties at 40% as at 30%. C.f. claim 20. Excipients, such as a component solvent that may be, for example, triacetin or NMP, are present in the composition of the art. Claims 16 – 19. A solubility modifier, pore former, emulsifier, or osmotic agent may also be present. Claims 4 – 7.

(a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 1 – 7, 10 – 13, 18 – 20, 22 - 39, and 40 - 53, 57 - 72 and 122 rejected under 35 U.S.C. 103(a) as being unpatentable WO 238185 (185 or the 185 reference) of record, in view of US 6,432,415 to Osborne, of record.

The limitations of most of the claims have been discussed above.

Claim 13 ultimately depends on claim 1, and requires the solvent benzyl alcohol. Claim 53 ultimately depends on claim 40, and requires a benzyl alcohol.

Claims 36 - 39 require particular particle sizes of the active agent.

Claim 122 requires a kit, wherein the kit contains a gel vehicle comprising a low molecular weight bioerodibe polymer, a water-immiscible solvent in amount sufficient to

form a gel with the polymer, and an anesthetic dissolved or dispersed in the gel. One or more additional materials, such as an excipient, are also required. The kit requires that the anesthetic agent be separated from the solvent until the time of administration to the subject.

The 185 reference discloses an injectable gel composition that provides sustained release of an active at the site of injection. Examples. The polymer may be PLGA. Claim 4. The PLGA may have carboxylic acid end groups. Example 2. The solvent polymer ratio is commensurate with the instant claims. See Example 2 (45% by weight polymer in solvent). The solvent may be benzyl alcohol. Claim 7. The polymer may be a 50:50 lactide:glycolide polymer with a molecular weight of about 5,000. Example 2 (a molecular weight of 6,000 is about 5,000). The PLGA has either acid or ester end groups, or a mixture thereof, depending on the desired method of polymerization. Page 13. The system is readily injectable through a 20 gauge needle, and the beneficial agent, which is dispersed as particles. Examples 2 and 3. The composition may be a kit having the beneficial agent in a separate container from the other agents, such as the solvent. Claims 38 – 45. The excipient and solubility modifier polyethylene glycol, is added in some embodiments. Example 3. Delivery of the agent occurs, for example, over one or three days. Example 6.

What is lacking is:

1) A beneficial agent that is an anesthetic, and

2) The specific particle sizes of claims 36 – 39.

Osborne teaches gel forming compositions based on PLGA. Claims 1 and 8. Osborne suggests the use of an anesthetic in such compositions. Claim 5.

It would have been prima facie obvious to a person of ordinary skill in the art at the time of the invention to incorporate an analgesic in the composition of 185. Doing so is merely following the suggestion of Osborne, who recognizes analgesics to be useful in similar compositions. The amount of anesthetic (instant claims 29 - 31 and 60 - 62) is a matter of dosing, which is routine optimization. It would have been prima facie obvious to a person of ordinary skill in the art at the time of the invention to optimize the particle size. The particle size will clearly depend on the needle through which the composition of '185 needs to pass. Thus, the artisan will optimize the particle size to be large enough to be readily manufactured and handled, but small enough to pass through the desired needle.

Claims 1 – 13, 18 – 20, 22 – 53, 57 – 72, and 122 are rejected under 35 U.S.C. 103(a) as being unpatentable over WO 238185 (185 or the 185 reference) of record, in view of US 6,432,415 to Osborne, as applied to claims 1 – 7, 10 – 13, 18 – 20, 22 - 39, and 40 - 53, 57 - 72 and 122 and in further view of US 5,614,206 to Randolph.

What is lacking from 185 and Osborne are the anesthetics of the instant claims, such as bipivacaine.

Randolph teaches that bipivacaine is an anesthetic suitable for formulation in a sustained release formulation. Claims 12, 20, and 26.

It would have been prima facie obvious to a person of ordinary skill in the art at the time of the invention to use bipivacaine as the drug in 185 and Osborne. Based on

the teachings of the art, the use of an anesthetic, particularly bipivacaine, in 185's composition is merely a combination of known elements leading to predictable results. The general composition of the claims is known, see 185 as applied above, but without anesthetics. Osborne shows that anesthetics are useful in related compositions, and suggests their use. Bipivacaine is an anesthetic. The Bipivacaine in the invention functions in the same way as in the art, namely by providing its recognized benefit. The dosage form carrying the bipivacaine also functions identically in the claims as in the art, namely by delivering an active in a sustained release manner. The combination gives no more than predictable results, and is therefore prime facie obvious.

Conclusion

No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Eric E. Silverman, PhD whose telephone number is (571)272-5549. The examiner can normally be reached on Monday to Thursday 7:00 am to 5:00 pm and Friday 7:00 am to noon.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael Hartley can be reached on 571 272 0616. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Michael G. Hartley/
Supervisory Patent Examiner, Art Unit 1618

/Eric E Silverman, PhD/
Examiner, Art Unit 1618